

BMJ Open Developing a model for decision-making around antibiotic prescribing for patients with COVID-19 pneumonia in acute NHS hospitals during the first wave of the COVID-19 pandemic: qualitative results from the Procalcitonin Evaluation of Antibiotic use in COVID-19 Hospitalised patients (PEACH Study)

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



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ABSTRACT

Objective To explore and model factors affecting antibiotic prescribing decision-making early in the pandemic.

Design Semistructured qualitative interview study.

Setting National Health Service (NHS) trusts/health boards in England and Wales.

Participants Clinicians from NHS trusts/health boards in England and Wales.

Method Individual semistructured interviews were conducted with clinicians in six NHS trusts/health boards in England and Wales as part of the Procalcitonin Evaluation of Antibiotic use in COVID-19 Hospitalised patients study, a wider study that included statistical analysis of procalcitonin (PCT) use in hospitals during the first wave of the pandemic. Thematic analysis was used to identify key factors influencing antibiotic prescribing decisions for patients with COVID-19 pneumonia during the first wave of the pandemic (March to May 2020), including how much influence PCT test results had on these decisions.

Results During the first wave of the pandemic, recommendations to prescribe antibiotics for patients with COVID-19 pneumonia were based on concerns about secondary bacterial infections. However, as clinicians gained more experience with COVID-19, they reported increasing confidence in their ability to distinguish

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This study adds to the evidence base on the complex factors influencing antibiotic prescribing decisions.
- ⇒ Findings have significant implications for health-care providers, policymakers and researchers in the ongoing efforts to combat rising antimicrobial resistance.
- ⇒ Some interviews were conducted up to a year following the events, which may have resulted in recall bias.
- ⇒ Understanding of current treatments for COVID-19 rapidly evolved during the early waves, which may have impacted the accuracy of information provided by interviewees.

between symptoms and signs caused by SARS-CoV-2 viral infection alone, and secondary bacterial infections. Antibiotic prescribing decisions were influenced by factors such as clinician experience, confidence, senior support, situational factors and organisational influences. A decision-making model was developed.

Conclusion This study provides insight into the decision-making process around antibiotic prescribing for patients with COVID-19 pneumonia during the first wave of the pandemic. The importance of clinician experience and of

senior review of decisions as factors in optimising antibiotic stewardship is highlighted. In addition, situational and organisational factors were identified that could be optimised. The model presented in the study can be used as a tool to aid understanding of the complexity of the decision-making process around antibiotic prescribing and planning antimicrobial stewardship support in the context of a pandemic.

Trial registration number ISRCTN66682918.

INTRODUCTION

Although COVID-19 pneumonia is a viral illness caused by SARS-CoV-2, many patients admitted to hospital during the first wave were prescribed antibiotics to treat suspected bacterial coinfection.¹ This led to an increase in antibiotic use for hospitalised patients. Accumulating antibiotic resistance is a major global threat to health and optimal antimicrobial stewardship (AMS) is paramount. Although targeted interventions, informed by theory and context-specific research, are needed to improve antibiotic stewardship,² empirical, contextual, qualitative research is limited for antibiotic prescribing in COVID-19. The unique context around the first wave of the pandemic has been well described, and includes a rapid increase in patient volume and change in patient mix, lack of information about a new disease, changes in diagnostic supplies and personal protective equipment (PPE) availability and deployment of healthcare workers to areas they were unfamiliar with.³

A qualitative study conducted in the UK found that general practitioners felt they had a lower threshold for prescribing antibiotics during the early pandemic, influenced broadly by patient presentation and changes to their working environment (eg, remote consultation⁴). Clinicians were also more likely to prescribe antibiotics when there was diagnostic uncertainty, when patients had severe disease or when there were multiple comorbidities.⁵

It is already known that an interplay of multiple complex factors can influence decision-making around antibiotic prescribing for adults with acute conditions in primary care settings.⁶ One systematic review⁷ found that decision-making tools can be useful in supporting antibiotic prescribing; however, in other studies, decision-making tools have been framed as an imposition on clinical autonomy among some medical specialists, creating a barrier to their use.⁸ Fontela *et al*⁹ examined factors influencing antibiotic-related decisions in paediatric intensive care units and highlighted a combination of factors, including clinical reasoning using an analytical approach to determine the likelihood of bacterial infection, disease severity, patient safety and intuition.

Early review and appropriate discontinuation of antibiotics is an important component of AMS processes. In the pre-COVID-19 era, Roope *et al*¹⁰ undertook a 'choice' survey with 100 practitioners to understand factors affecting discontinuation of antibiotics. They concluded it was a complex process, with much variation between clinicians, but that consultants were more likely to discontinue than more junior respondents. In routine practice, fewer than 10% of initial antibiotic prescriptions among

acute medical admissions are discontinued, while up to 20–30% could be stopped safely (Walker *et al*, 2019; Islam *et al*, 2018; Fawcett *et al*, 2016, cited by ref 10). Sociocultural and behavioural factors, such as fear of adverse health outcomes for patients and beliefs about the applicability of antibiotic prescribing guidelines, are likely to play a role in these decisions. Roope *et al*¹⁰ concluded that revising antibiotic guidelines to be less prescriptive about duration and making duration conditional on patient factors and treatment response could help safely increase the frequency of early discontinuation of antibiotics in hospitals. Al-Azzawi *et al*¹¹ highlight the need for context to be taken into account in theories of medical decision-making, which would impact education, clinical practice and policymaking. However, there is no universally accepted definition of context in medical terms.

Inflammatory markers have been identified as a factor influencing antibiotic prescribing in hospitalised patients with COVID-19.⁵ The Procalcitonin Evaluation of Antibiotic use in COVID-19 Hospitalised patients (PEACH Study) focused on the impact of procalcitonin (PCT) on antibiotic prescribing during the first wave. PCT is a biomarker that was being used prior to the pandemic to help clinicians distinguish between bacterial and viral infections and guide antimicrobial prescribing. Several studies have shown that using PCT to guide antibiotic treatment can safely reduce antibiotic use and minimise antimicrobial adverse effects in patients with respiratory infections and sepsis.¹² O'Riordan *et al*⁸ conducted a process evaluation of the use of PCT as a biomarker to support prescribing decisions and reduce antimicrobial use safely in patients with respiratory tract infections. The positive impact of PCT on reducing antimicrobial prescribing was reported, but variability in the use and adherence to PCT testing protocols was noted, suggesting the need to explore factors influencing implementation for improved effectiveness of interventions. The initial version of the National Institute for Health and Care Excellence (NICE) COVID-19 rapid guideline (NG191; NICE, 2022¹³) stated that there was insufficient evidence to recommend PCT in COVID-19 pneumonia.

Procalcitonin tests could be useful in identifying whether there is a bacterial infection. However, it is not clear whether they add benefit beyond what is suggested in the recommendation on tests to help differentiate between viral and bacterial pneumonia to guide decisions about antibiotics. The most appropriate threshold for procalcitonin is also uncertain. (p 28)

The guidelines encourage centres already using PCT to participate in research.

Research objectives

To explore the decision-making process around the use of antibiotics in the management of hospitalised patients with COVID-19 pneumonia during the first wave of the

pandemic, in hospitals that did or did not use, or introduced PCT testing during the first wave.

METHODS

Design

The study is based on a thematic analysis¹⁴ of interviews with 29 clinicians who worked during the first wave of the COVID-19 pandemic (defined here as March to June 2020) from six National Health Service (NHS) acute hospital trusts and health boards from England and Wales that took part in the PEACH Study. PEACH is a mixed-methods programme of work including a retrospective observational cohort study using patient-level clinical data from acute hospital trusts and health boards in England and Wales.^{15–17} The primary objective was to measure the difference in antibiotic use between patients with COVID-19 pneumonia who did or did not have PCT testing at the time of admission, to assess whether the use of PCT testing, to guide antibiotic prescribing, safely reduced antibiotic use among patients who were hospitalised with COVID-19 during the first wave of the pandemic. The qualitative interviews with clinicians were designed to explore the decision-making process around the use of antibiotics in management of patients with COVID-19 pneumonia. Although the term ‘pneumonia’ might imply severe illness, a spectrum of severity was included in the discussions with clinicians.

Inclusion criteria for the qualitative component of this study comprised: (1) clinicians who had cared for patients with COVID-19 pneumonia working at one of the six selected sites during the period March to June 2020 and (2) had some experience or responsibility for antibiotic decision-making either alone or within a team.

Procedure

Recruitment

We selected six sites that either routinely used PCT testing before and during the pandemic, introduced PCT testing during the first wave of the pandemic or did not use PCT testing either before or during the first wave of the pandemic. Two were selected from each category. Hospitals differed in their policies around PCT due to the lack of direction in the national guidelines at the time, leaving it to local discretion.

Interview participants were clinicians who had cared for patients with COVID-19 at one of the six selected sites during the period March to June 2020, and had some experience or responsibility for antibiotic decision-making either alone or within a team.

Participants were sampled with maximum variation across (a) role (eg, consultant/specialty trainee/nurse specialist/pharmacist, aiming to include at least one of each role from each site) and (b) hospital site (comparing sites that routinely used PCT, those that did not and those that introduced PCT during the first wave of the pandemic).¹⁶

Participant information sheets and expressions of interest for the qualitative interviews were disseminated to managers of departments within the six sites via email by the site principal investigators. Potential participants returned a consent to contact form and were contacted by the PEACH qualitative researcher to arrange an interview. In the UK, and in accordance with the General Data Protection Regulation 2016/679, researchers cannot record personal information including contact details from a third party without consent of the individual. Therefore, in studies where participants are recruited indirectly, a consent to contact form must be used for the potential participant to demonstrate that they are willing to be contacted by the researcher. Informed consent was taken over the phone and recorded by the qualitative researcher (consent script included in the online supplemental information).

Data collection methods and instruments

A topic guide was developed with input from the PEACH multidisciplinary management team and the patient and public involvement (PPI) advisory panel.

Our target was to conduct up to five interviews per participating NHS trust, thus giving greater breadth of practice variation. This is based on our previous qualitative research on clinicians and patients’ perspectives on antibiotic resistance and infection management, where 15–30 were found to be sufficient based on previous studies.^{18–20}

Semistructured interviews with clinicians at study sites were conducted virtually in line with good practice to reduce COVID-19 transmission. Participants were interviewed in their workplaces and some in their own homes on days they were not in work. Interviews were carried out between August 2021 and November 2021.

We asked clinicians to reflect on their practice during the first wave of COVID-19. We examined the use of PCT in guiding antibiotic decisions for centres that routinely used it. We also explored the reasons for adherence or non-adherence to testing algorithms and gathered feedback on potential changes to those algorithms. For centres that did not use PCT or algorithms, we investigated how clinicians might use tests/algorithms to inform antibiotic prescribing for patients with COVID-19 pneumonia. We explored the use of PCT and testing algorithms in guiding antibiotic decisions, as well as the impact of the NICE COVID-19 rapid guideline¹³ on PCT use. A hypothetical scenario was presented to elicit factors influencing decision-making, including clinical and non-clinical influences. The full topic guide can be found in the online supplemental information.

The topic guide was flexible, giving interviewees control over the order and wording of questions. They had the freedom to introduce and discuss topics beyond the prepared material. The interviews followed a conversational approach, allowing participants to guide the extent and order of questions. Participants were encouraged to raise any additional aspects of the pandemic and



antibiotic stewardship that were personally significant, shaping the interviews according to their perspectives.

Data analysis

Interview recordings were transcribed and anonymised. Interview transcripts were analysed using a five-stage framework approach²¹ to account for the different interviewee characteristics, for example, PCT used/not used or introduced during the first wave, grade of clinician, etc. Analysis was thematic, seeking to identify common themes, patterns and meanings within the data.¹⁴

Following an initial process of familiarisation by reading and re-reading the transcripts, and line-by-line coding (using NVivo V.12²²), tentative 'overarching' themes were generated, which were then reviewed and refined into subthemes. The thematic framework was based on the research objectives and emerging themes. After applying the thematic framework ('indexing'), the fourth stage, 'charting', involved retrieving the coded data and producing summaries of interviewees' talk produced on each theme, for each individual participant, and visually arranging it in a table to build an overall picture of the whole data set. This allowed easier comparison across clinicians and hospital sites to identify variation and similarities in the final stage of interpretation of data. The fifth stage, 'mapping', involved the research team using the charts to map and interpret the data set as a whole and connect with the original research objectives.

Rigour was ensured in two ways. First, two researchers (JH and LB-H) conducted the thematic analysis process for 20% of transcripts, improving internal validity. Meetings were set up between these researchers and the PPI representative (MO) to discuss 10% of transcripts and the coding framework. MO has previous experience of qualitative research methods as a PPI representative. She provided a third point of view on the data as a way of increasing rigour. Themes were compared, discussed and agreed, and an iterative process of discussion and verification within the research team enhanced external validity.

Decision-making matrix

Following the generation of themes, a model of decision-making, using a matrix to represent the complexity of input into the decision, was proposed and refined within the team. This model is presented here, with themes used to describe the model. The decision-making matrix was developed using the Eisenhower matrix as a base,²³ including three variables: acuity, vulnerability and likelihood. Themes are presented before the matrix and referred to within the discussion of the matrix.

The Eisenhower matrix is a decision-making tool that helps people prioritise tasks based on their urgency and importance. Tasks are categorised into four quadrants: urgent and important; important but not urgent; urgent but not important; and not urgent and not important.²³ The simplicity of the four quadrants can be useful in prioritisation of patients as well as tasks. The matrix has been adapted in healthcare decision-making by using the

original spectra of urgency and importance (eg, ref^{22 24}), and by substituting other spectra, for example, effort in place of urgency.²⁵ However, a four-quadrant model has also been criticised as being too simple for more complex decision-making processes.²⁶

Patient and public involvement

Patient and public representatives were involved during all stages of this research, as part of the overall PEACH study.

FINDINGS

We received 32 consent to contact forms and interviewed five clinicians in five of the sites, and four in the sixth site. Interviewees comprised 15 medical consultants; 7 non-consultant physicians; 5 lead or specialist pharmacists; and 2 specialist nurses. Of the consultants, four had been consultants for over 10 years, six between 6 and 10 years and five between 0 and 5 years, with some very recently appointed as a consultant. Of the non-consultant physicians, three had been qualified ≤ 5 years and four more than 5 years. Some participants had experience from different hospitals within and outside the UK, and others solely from within the one hospital. We captured other characteristics, such as gender; however, as these were not evenly distributed, reporting them would risk identifying the participants.

The mean interview length was 40.97 min (range=19–65.5 min) excluding the consent recording.

Themes were found to be cross-cutting across all participants (in terms of job role and site) and were relevant to addressing the central study aim of exploring decision-making process around the use of antibiotics in management of patients with COVID-19 pneumonia. Thus, final theme generation considered the data as an integrated corpus. Themes arising from the interviews include (1) clinician experience, confidence and support, (2) situational factors and (3) organisational influences (see [table 1](#) for table of themes).

Clinician experience, confidence and support

Challenges of decision-making in the face of a new disease

During the early stages of the COVID-19 pandemic, clinicians had difficulty distinguishing between signs and symptoms due to SARS-CoV-2 viral infection and those due to secondary bacterial infections, leading to some clinicians prescribing antibiotics unnecessarily. However, as the pandemic progressed, clinicians gained more experience and gained confidence at distinguishing between the two. They used clinical features, such as the pathology of the lungs as determined by chest radiographs, ultrasound scans or CT scans, to differentiate between infections due to SARS-CoV-2 and bacterial infections. Clinicians also felt that they were less likely to prescribe antibiotics except in cases where additional bacterial infection was more likely present, and they adjusted their prescribing decisions based on symptoms that did not fit the typical COVID-19

Table 1 Themes influencing antibiotic prescribing decisions

Theme	Subthemes
Clinician experience, confidence and support	Challenges of decision-making in the face of a new disease
	Clinician seniority
	Clinicians' attitude to risk
	Clinicians' attitude to antimicrobial stewardship
Situational factors	Clinicians' feelings of helplessness—new disease and no specific treatments
	Timing of initial prescription
	Availability of resources
	The role of laboratory tests <ul style="list-style-type: none"> ▶ Introducing the PCT test in a new context ▶ How the tests contribute to the decision ▶ The role of PCT and other blood tests in reviewing and stopping antibiotics ▶ How laboratory tests were integrated into protocolised care
	Evidence-based guidelines
Organisational influences	Where a patient sits on the patient journey
	Evidence-based guidelines

PCT, procalcitonin.

pneumonia pattern. Some clinicians reported that antibiotics were being prescribed more readily, '*like smarties*' (P07, Consultant, Did not use PCT before or during the first wave), during the first wave of the pandemic due to the lack of available treatments for COVID-19, despite their better judgement.

Looking back to April 2020... I think if anyone was unwell enough to need oxygen, they were getting antibiotics. Everyone had a feeling that they had COVID and the chances of them having a superadded bacterial infection was unlikely, and this [their condition] was because of COVID. But I think it felt like one of the very few things that we could do, so even though part of us was going they shouldn't be on antibiotics, then this might contribute to antimicrobial resistance, and there's many reasons why we shouldn't be doing this. Certainly, in the beginning it was blanket coverage for everyone. (P21, Non-consultant physician, Introduced PCT during the first wave)

There were absolutely no treatments for COVID in wave one, that's probably another thing that perhaps lowered the threshold for giving antibiotics... Even if you're saying to yourself well there's only a five or ten percent chance that there is a bacterial infection, in that situation the temptation is very much to use some antibiotic, even though you think it almost

certainly won't help. (P20, Consultant, Introduced PCT during the first wave)

Clinician seniority

Clinicians with more experience and expertise in respiratory infections were more confident in their prescribing decisions. Factors such as the clinician's area of expertise, confidence in their ability to identify a bacterial chest infection and seniority also played a role in their decision-making process. Junior colleagues tended to seek guidance from more senior colleagues when making decisions about antibiotic prescriptions. The availability of senior staff was seen as crucial to the decision, indicating that seniority was considered by participants to be key to making the right decision. Clinical judgement, experience and luck were identified as key factors in making informed prescribing decisions.

Medicine is always weighing competing probabilities, ...it's more difficult when one test, or one feature says one thing, and another test will feature if the patient's condition says something completely different. And, that's when you need experience, judgement, and luck to make the right decision. (P20, Consultant, Introduced PCT during the first wave)

Antibiotic use did decrease over the time... because we had more information, more evidence base and because... care was consultant led. It's very rare that junior doctors will start and stop antibiotics, really and it's quite often done by the consultants. (P12, Consultant, Used PCT before and during the first wave)

Clinician's attitude to risk

The emotional impact of making complex decisions regarding antibiotics and other treatments has a powerful effect on clinicians and their colleagues, leading to a risk-averse attitude. Participants acknowledged that in hindsight, they and their colleagues probably overprescribed antibiotics due to working with limited information about a new disease, at the time. At the outset of the pandemic, broad-spectrum antibiotics were prescribed to all patients, but the practice changed as more information became available.

Not offering certain therapy... is an incredibly difficult decision and I know has affected a lot of my colleagues including myself, a lot. I have cases where looking back I don't think between us all we got the balance right. Both ways. People who shouldn't have been put on ventilators and died horrendously, and people that should have been put on ventilators and died probably sooner than they might have because they may have responded to a ventilator, or to an intensive care environment. However, these are not black and white decisions, they are very complex

decisions. (P29, Non-consultant physician, Did not use PCT before or during the first wave)

Clinician's attitude to AMS

Participants had differing attitudes towards antibiotic stewardship during the first wave of the COVID-19 pandemic. Some justified the increased use of antibiotics due to the lack of knowledge and treatments available, while others questioned it in retrospect but understood the extreme circumstances. Despite this, clinicians were mindful of sepsis and AMS training, and antibiotics were sometimes used even though they were unlikely to help the patient. The use of antibiotics was guided by the same principles as usual clinical practice for some participants, while others cited research and advice suggesting a higher incidence of secondary bacterial infections during COVID-19. Sepsis was noted by several participants as being at the forefront of their minds when prescribing antibiotics, even if there were contraindications to their use, such as *Clostridioides difficile*.

I think the blanket presumption has to be that where you see a clinical potential indication you have to give them [antibiotics], and in the absence of any evidence base with a novel infectious disease I think it comes down to almost the art form of medicine, senior clinicians doing what they think is right. That is reflected in the WHO's pandemic or novel infectious diseases guidelines under permitted emergency use. It comes down to whether or not there is a reasonable opinion amongst peers that the intervention may have benefit. I think with antibiotics it would be difficult to argue that that wasn't the case at the beginning. (P29, Non-consultant physician, Did not use PCT before or during the first wave)

Clinicians' feelings of helplessness: new disease and no specific treatments

Participants described the emotional burden felt by clinicians when deciding whether or not to prescribe antibiotics during the COVID-19 pandemic. Some participants expressed feelings of helplessness and pressure to do everything possible to help critically ill patients, which sometimes led to overprescription of antibiotics. Despite acknowledging the risks of overprescribing, some clinicians admitted to prescribing antibiotics out of a personal need to do something rather than nothing.

We needed to do everything we could to help these patients. I think that's where the stewardship kind of goes out the window. You can totally get it, it's just emotion, isn't it? (P27, Pharmacist, Did not use PCT before or during the first wave)

The patients that looked like they had COVID, but were doing badly, the ones that looked like they were going to die, is extremely difficult to stop antibiotics in those patients... let's just give them that,

and then at least we know that we haven't neglected something that could have made a difference. (P06, Non-consultant physician, Did not use PCT before or during the first wave)

Situational factors

Timing of initial prescription

During overnight shifts, there are fewer senior staff members available, and test results are less likely to be returned, making it difficult for night staff to make informed decisions about antibiotic prescribing. This left them feeling isolated with less support for challenging decisions compared with daytime admissions.

In the middle of the night, when I was on call, I never waited for any blood results to come back, we just had to take that decision on the basis of the clinical picture at that time. So out-of-hours... I wouldn't wait for the next four hours to take that decision. I would just put them on antibiotics. (P03, Non-consultant physician, Used PCT before and during the first wave)

Availability of resources

The participants discussed the challenges of working in an overstretched healthcare system during the first wave of the pandemic, which affected their decision-making around prescribing antibiotics. They highlighted the issues of limited nursing capacity (due to high nurse to patient ratios and staff sickness) for administering intravenous antibiotics several times a day, limited space for preparing and administering intravenous antibiotics due to increased patient numbers and concerns about the availability of therapeutic interventions such as oxygen and antibiotics. Participants also reported concerns over the use of PPE during the pandemic, which paradoxically might lead to a greater infection risk due to lack of hand hygiene and not changing PPE between patients. Overall, the decision-making process was influenced by what worked for the organisation rather than solely for the patients.

On a general medical ward, you could be talking about one trained nurse to you know, 12, 15, maybe even more, patients, at times. So, one implication of that is, it's extremely difficult to give IV antibiotics that are given multiple times a day... 20 minutes three times a day, per patient, making up IV antibiotics, and then another 20 min administering them, well you do the maths, that doesn't add up... there would be times where I would be maybe have given IV antibiotics but didn't, because I didn't really believe it was a bacterial infection, and I thought this is not where we should be prioritising nursing care. (P06, Non-consultant physician, Did not use PCT before or during the first wave)

Because we were gloved and gowned in full PPE, people weren't swapping gloves in the same way because

you've got visual clues... I think there were things like that that meant secondary bacterial infection became more of an issue. (P13, Consultant, Used PCT before and during the first wave)

The role of laboratory tests

Introducing the PCT test in a new context

These interviews examined the introduction of PCT testing in a new context, and participants expressed both confidence and concern in using the test. While most used PCT testing as one factor in decision-making, some worried about over-reliance on the test result and suggested training to interpret results. The absence of PCT testing may have led to more antibiotic prescriptions, especially in the early days of the pandemic when mortality rates were high.

I think people weren't totally sure. Some people debated whether the Procalcitonin is as good as it's meant to be. And, I think there's a little bit of uncertainty about that. If anyone was caught out ever, then that would probably have a significant influence on delays and tests where you're not going to change. If you haven't got a result of a test, you're not going to act on it. (P18, Consultant, Introduced PCT during the first wave)

If someone has come in with shortness of breath, and within 10 minutes you are doing ECGs, you are listening to the chest, you might be organising x-rays and blood tests. The differential is quite wide... nearly everybody gets started on antibiotics unless it's an obvious cardiac reason. And I think the PCT test has actually been really quite useful in helping guide, whether or not you continue on those antibiotics when you look at... obviously you look at the palpation, you are looking at the CRP [C-Reactive Protein], the white cell count, you look at the temperature, you look at them clinically. But I think I think PCT has actually added quite a bit to our knowledge. (P16, Pharmacist, Introduced PCT during the first wave)

How the tests contribute to the decision

Participants mentioned the challenges of delays in receiving PCT test results and the integration of laboratory tests into routine hospital practices. Some participants expressed confidence in the usefulness of PCT testing, while others suggested that further tests were needed before prescribing antibiotics. Clinicians also talked about the technicalities of weighing the risk of a patient having an infection or not based on the evidence before and after the PCT test results.

If we didn't have this test that could help guide us, I think personally I would have given everyone antibiotics, complete for five days, and felt safe knowing that I've given them the maximum treatment, especially with such a high mortality initially. So, I think

yeah definitely a useful test, and definitely one that helps guide physicians in a safe way. (P24, Consultant, Introduced PCT during the first wave)

Collectively we've got a sense of confidence that the test actually is reasonably robust and tells you something that is, in most situations, reliable... The use is, I'm sure, increasing, [this] tells you that a lot of people have weighed it up and think, okay this is something that's reasonably reliable and useful. (P20, Consultant, Introduced PCT during the first wave)

The role of PCT and other blood tests in reviewing and stopping antibiotics

Some clinicians may prescribe antibiotics based on initial information before laboratory test results are available, and decisions to stop antibiotics may be made by someone else later on. There were a lot of tests being performed (such as D-dimer, prothrombin time and fibrinogen), which many clinicians had limited experience of interpreting in the context of a new disease, which may have complicated rather than supported clinical decision-making. Most clinicians stated that routine practice was to prescribe antibiotics on admission if there were signs of infection, and review and potentially stop them before the full course was complete. However, some participants reported that once a patient was on a course of antibiotics, they were likely to complete the full course. The introduction of PCT testing was seen as beneficial as it gave an extra piece of evidence to reduce the duration of antibiotics in a patient who would otherwise have finished the initial planned course.

The PCT takes twenty-four hours or so to come back, and you don't have twenty-four hours to make the decision about whether or not to start them on antibiotics. So, you make that decision the moment that patient comes in based on the history, the examination, and the test that you get back quickly such as the chest x-ray and symptom biochemistry, and then as you spend more time with the patient over the next twenty-four, forty-eight hours, you just get a feel for what's going on and you use that feel plus the PCT to make decisions going forward. (P04, Non-consultant physician, Used PCT before and during the first wave)

Especially that first wave, it was just really frustrating, because we were told to do so many different laboratory tests – lots and lots of tests, blood tests – and some of them which muddied the water... I'm fairly sure blood tests didn't play a role at all in the decision to give antibiotics. It was based on clinical severity. (P10, Consultant, Did not use PCT before or during the first wave)

How laboratory tests were integrated into protocolised care

During the first wave of the pandemic, a specific set of laboratory tests on admission with suspected COVID-19

pneumonia were introduced, as well as daily blood tests for infection markers such as CRP. This routine became standard practice for clinicians to monitor patients' response to antibiotics.

We segregated the admission pathway into green and red according to whether COVID was suspected or not suspected. And, people going down the red pathway then really did get quite protocolised care, they all had the same investigations, including a procalcitonin and a d-dimer, a ferritin, LDH, chest x-rays. (P20, Consultant, Introduced PCT during the first wave)

Organisational influences

Where a patient sits on the patient journey

The discussion focused on the process of how patients moved through the hospital, from initial assessment in the emergency department (ED) to admission to a ward where they are reviewed and reassessed by different practitioners. Some clinicians, in ED, for example, only initiated antibiotics and were unlikely to review them at 48 or 72 hours, while others were more likely to see patients later in their journey through the hospital. Participants who worked in the early stages of this journey reported prescribing antibiotics as a matter of course, as per hospital policy, assuming that they may be stopped once test results were returned. During the first wave of the pandemic, some hospital guidelines mandated that antibiotics be prescribed to patients with severe COVID-19 pneumonia on admission as part of a '*package of COVID therapy*' (P25, Consultant, Did not use PCT before or during the first wave). Clinicians who worked with patients in later stages of their journey through the hospital structure talked about patients who had been prescribed antibiotics on arrival, and how this impacted on their decisions.

A lot of the role in the Emergency Department is making sure that you have done the right tests and investigations that allow others to do that job forty-eight hours down the line. So, within the ED... you get a relatively broad remit of being able to start broad-spectrum antibiotics quite freely... So, my role doesn't really involve the stopping of antibiotics. It involves a lot of the starting of antibiotics and a lot of the assurance and investigations to make sure that others can do the stopping at the right point. (P02, Consultant, Used PCT before and during the first wave)

Someone has had their initial antibiotics at the front door, you have got a few hours before you need to make a decision about whether to continue or stop. So, we would often ... we would wait for the blood test results to come back. (P23, Consultant, Introduced PCT during the first wave)

Evidence-based guidelines

During the first wave of the pandemic, healthcare professionals lacked confidence in the guidelines provided due to their questionable evidence base and the rapidly evolving guidance. Some guidelines were based on the opinions of senior clinicians rather than randomised controlled trial evidence, resulting in different practices between teams and health boards. This led to discussions and interpretations of emerging literature on COVID-19 management among healthcare professionals.

A lot of the guidelines were, I suppose, European white male, senior clinician says this is what we need to do. And it's just opinion, rather than having either an observation or a randomised control trial evidence base. And so we were, at the time we were sort of ping-pong lots of the papers between each other in WhatsApp groups. And should we do this, should we do that? (P26, Consultant, Did not use PCT before or during the first wave)

Matrix development and interpretation

Clinical decisions about prescribing antibiotics for COVID-19 are incredibly complex: clinicians are synthesising a large amount of information, which includes (but is not limited to) the acuity of the illness (how sick they are), the vulnerability of the patient to infection (age, immunosuppression, risk factors, etc) and the likelihood of bacterial infection (based on clinical signs, laboratory tests and radiology). This study sought to understand how PCT may have influenced antibiotic prescribing in the complexity of these decisions. We took the original Eisenhower matrix and adapted it to suit our data.

A schematic of the factors influencing antibiotic decisions is presented in [figure 1](#).

We have adapted the Eisenhower matrix²³ to create a descriptive model for prescribing antibiotics. Calculating an exact probability of prescribing would be difficult due to the many factors involved. The model we developed has moved away from the simple quadrant design of the Eisenhower matrix. However, it is possible to map our ideas onto the original matrix.

Colour mapping represents the likelihood of prescribing antibiotics based on various factors, including clinician experience, hospital organisation, resource availability and patient influx. The decision-making process is not always straightforward and may have outliers.

In this section, we present examples of the model in action, where themes arose from the case studies presented, or from spontaneous responses to more general questions. Examples include low and high likelihood of prescribing antibiotics (less perceived risk, less likely to prescribe antibiotics; more perceived risk, more likely to prescribe antibiotics).

In the low likelihood scenario, a senior consultant with expertise in treating patients with COVID-19 would only prescribe antibiotics if there were clear signs of a bacterial infection or if the patient was particularly vulnerable.

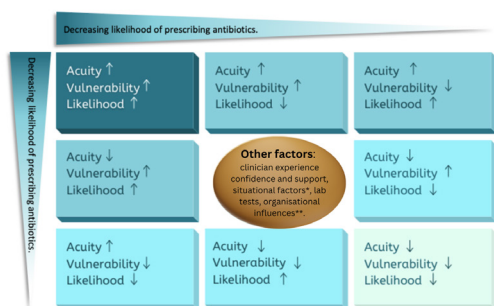


Figure 1 The complex factors which influence decisions to prescribe antibiotics. The blue boxes indicate the combination of factors contributing to the likelihood of prescribing antibiotics. The three main factors are: the acuity of the illness (how sick they are), the vulnerability of the patient to infection (age, immunosuppression, risk factors) and the likelihood of bacterial infection (based on clinical signs, laboratory tests and radiology). Other factors: clinician experience, confidence and support; situational factors; laboratory tests; organisational influences. The directional colour scale (orange) indicates the likelihood for prescribing antibiotics, with darker shaded areas weighted towards a higher likelihood of prescribing, and areas of lighter shading towards lower likelihood of prescribing. *Situational factors include time of day, family/patient pressure to prescribe antibiotics, etc. (The question of how much impact family/patient pressure had on decision-making was presented to clinicians during the interviews. The majority expressed that they were senior and confident enough to ignore pressure to prescribe, which could be expressed during telephone calls from relatives. However, they might take patient wishes into consideration in terms of intolerances or preferences against particular antibiotics.) **Organisational factors include staffing levels, busyness of emergency department (ED), availability of laboratory test results in real time, etc.

Exceptions to this approach would be rare and would be based on clinical judgement or ‘gut feeling’ (P28, Non-consultant physician, Did not use PCT before or during the first wave).

In the high likelihood scenario, a clinician would likely prescribe antibiotics if a patient was very unwell, or was vulnerable, and there was a high likelihood of bacterial infection based on clinical, laboratory and radiology findings.

I think people like that reassurance: they don’t think the patient needs it, but here’s a test that says actually, no, they don’t need it, so we can stop it. I think they always have that doubt in their mind. Unless they’ve got something which says, ‘Yes, you’re right. They don’t need it,’ they’ve still got that doubt and that pressure, I think, from family, from people who are saying how sick this patient is, to carry on with the antibiotics. (P09, Pharmacist, Did not use PCT before or during the first wave)

Some of the anaesthetists who came to help with the ICU mainly do a lot of their work in theatres so again

they are not used to seeing pyrexias of 40. The only other group [that] see that is in the head injury and neuro patients where they’ve got a lot of blood in their head which gives a pyrexia as well. So yes, so I think lots of inexperienced staff and a new disease meant that we probably started antibiotics earlier than they would have done anyway, and probably less ICU consultant decision-making in it. (P27, Pharmacist, Did not use PCT before or during the first wave)

During the early stages of the COVID-19 pandemic, clinicians lacked confidence in treating patients and prescribed antibiotics as a precautionary measure due to limited information and experience with the disease. Antibiotic use was more widespread, even for low-acuity and low-vulnerability patients, and external factors such as an overloaded system and hospital policy influenced prescribing decisions. Clinicians may have prescribed antibiotics as it was the only active treatment available, and they felt the need to do something for the patient. However, as more clinicians became experienced and shared their practice, prescribing became more straightforward. There was also a tendency to err on the side of caution and prescribe antibiotics rather than not prescribing, due to not wanting to make the wrong decision.

At the first wave, it was very tricky, because we didn’t have a handle on the disease. If I see somebody with a pneumonia... As well as the knowledge that I’ve read, I’ve got an instinct from having seen so many people with a pneumonia. You have that... I suppose it’s experience, isn’t it? Whereas when you were seeing patients with COVID, you just didn’t have that. So, they had really frightening-looking x-rays and they [patients] were just looking okay. But you were still really frightened, because you didn’t know what the trajectory was like. So you were quite heavily dependent on guidelines at that point, because you didn’t have your own acumen. (P10, Consultant, Did not use PCT before or during the first wave)

There was a lot of discussion in the very first couple of weeks when we knew this was coming, about whether we’d be recommending kind of antibiotics for everyone that was being admitted with COVID pneumonia. There was a range of opinions on that, but everyone had a pretty low threshold for suggesting antibiotics would be given during that first wave. (P06, Non-consultant physician, Did not use PCT before or during the first wave)

Our antibiotic usage was quite high, and probably still is in comparison to other years... we were just trying to kind of treat them with everything that we could... However, as more and more clinicians became experienced and shared their practice it became really straightforward. (P05, Pharmacist, Used PCT before and during the first wave)

DISCUSSION

This study aimed to explore how clinicians made decisions about prescribing antibiotics to patients with COVID-19 pneumonia during the first wave of the pandemic in the UK. Clinicians reported using a combination of clinical judgement and guidelines to make antibiotic decisions during the early stages of the pandemic.

Participants highlighted the challenge of distinguishing between infections due to SARS-CoV-2 virus and bacterial infections in the early stages of the first wave, leading to uncertainty around prescribing antibiotics. Hospital policy and practices, which were strained due to a high volume of critically ill patients, and were different from normal, influenced antibiotic prescribing decisions. Prescribing antibiotics on admission to patients with suspected COVID-19 pneumonia was a routine practice, and there was uncertainty and variability around the guidelines and protocols for the management of COVID-19 pneumonia. Additionally, the rapid movement of patients through the hospital system created challenges for some clinicians in terms of decision-making and continuity of care.

These findings led to the development of a conceptual model of decision-making. This model, as the interviews highlight, involves multiple, complex factors which contribute to the clinical decision to start antibiotics in patients presenting with COVID-19 pneumonia during the first wave.

In terms of use of PCT to inform antibiotic prescribing decisions, participants represented themselves in two ways: those who believed that PCT testing reinforces prescribing decisions already made versus those who believed it may support decisions to withhold antimicrobial initiation. A key difference in perception concerned timing of when the PCT result was used, to support antibiotic initiation or discontinuation. Some participants expressed concerns about protocolised interpretation and the need to over-ride results if discrepant with the assessment of acuity, vulnerability and likelihood of bacterial infection.

The findings of the current study relate to the previous literature on antibiotic prescribing in several ways and are largely consistent with limited studies from the COVID-19 pandemic.^{27 28} There are common factors in the decision-making process in our study and others as follows: diagnostic uncertainty, clinician experience and training, time and resource pressure⁶; hospital culture and organisation, fear and risk aversion⁸; intuition and gut feeling, junior staff deferring decisions to senior staff and the tendency to continue antibiotic treatment initiated by colleagues.⁹ Breakdown of usual AMS processes has been identified in previous studies, but this was only vaguely alluded to in the present study.³

Charani *et al*²⁹ found that 'prescribing etiquette' and the hierarchical culture within hospitals, where senior consultants are unquestioned and exempt from following policy, but rely on clinical judgement, while junior colleagues follow their lead, need to change before over-prescribing can be addressed.

Our study provides insight into the decision-making process which led to approximately 85% of patients admitted to the hospital with COVID-19 pneumonia during the first wave receiving at least one dose of antimicrobials, when the true bacterial coinfection rate was only 2.3%.³⁰ From our data, it is plausible that most clinicians operated in the context of a low threshold of prescribing antimicrobials, sometimes despite their better clinical judgement. The participants gave important insight into the organisational factors (availability, turnaround time and reliability of tests), in addition to the different personal and clinical motivational factors which influence everyday clinical decision-making in a stressed environment.

Limitations

One limitation of this study is that some interviews were conducted up to a year following the events, which may have resulted in recall bias. Interviewees expressed difficulty in remembering the details of the time period, which was characterised by chaos and uncertainty due to the emergence of a new disease. Another limitation is the exponential learning curve surrounding the disease, including how to treat it and determine whether antibiotics were beneficial for a viral infection that presented similarly to sepsis. This rapidly evolving understanding of the disease may have impacted the accuracy of information provided by interviewees during the study.

What this study adds

The study highlights that decision-making in the management of COVID-19 pneumonia during the first wave posed unique challenges due to the uncertainty surrounding the disease's nature and clinical course. We note that many interviews conducted for the study emphasise the impact of COVID-19 testing delays on decision-making, and that many practitioners described having to make decisions without confirmation of COVID-19 infection.

This study adds to the evidence on how antibiotic decisions are made in general, highlighting the importance of considering the unique challenges posed by new infectious diseases such as COVID-19. The findings have significant implications for healthcare providers, policy-makers and researchers in the ongoing efforts to combat rising antimicrobial resistance. By improving our understanding of the challenges involved in decision-making for antibiotics in the face of diagnostic uncertainty, such as occurred in the first wave of the pandemic, this study can inform the development of evidence-based guidelines and protocols for better management of pneumonia and other serious infections in adults admitted to hospital, and aid preparation for future pandemics.

CONCLUSION

Antibiotic prescribing decisions involved a complex interplay of factors known to influence antibiotic use, in combination with highly context-specific factors, like diagnostic

uncertainty, staffing levels and availability of resources, that often interfered with AMS. The complex process could be represented in a conceptual Eisenhower-style model that included clinical factors, acuity of illness and vulnerability. Other factors such as guidelines and availability of PCT testing influenced decisions. PCT testing was deemed useful by many clinicians treating patients with COVID-19 pneumonia, either through not initiating or earlier cessation of antibiotics. However, participants highlighted the need for rapid results, robust evidence for utility and training in the interpretation of results, in order for PCT to truly influence practice and prescribing decisions.

Overall, this study contributes to our understanding of antibiotic decision-making in general, the unique challenges posed by COVID-19, and can aid AMS planning for future pandemics.

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Contributors JH and LB-H are joint first authors and led the writing of the manuscript with input and critical review from all listed coauthors (JE, PP, ML, PH, NP, PD, TS, TPH, MA, RH, GP, MO, WM, JS, ET-J, EC). EC and JS are joint co-chief investigators. JH carried out clinician interviews. ET-J and EC are joint senior authors and provided overall supervision, leadership and advice. JS is the guarantor and accepts full responsibility for the finished work and/or the conduct of the study, had access to the data, and controlled the decision to publish. All members of the PEACH study team were involved in the design of the PEACH trial.

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Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Ethics approval The PEACH study protocol was approved by the HRA and NHS REC (West Midlands–Solihull Research Ethics Committee, reference: 21/WM/0052). This approval covered all workstreams listed in the protocol, including the qualitative study described in this paper. Registration number: ISRCTN66682918.

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CONSENT SCRIPT FOR QUALITATIVE STUDY

Please listen carefully to the following statements and say 'yes' or 'no' after each statement to confirm whether you agree.

1.	I confirm that I have read and understood the Information Sheet for Qualitative Study (version 1.1 dated 24/02/2021) for the PEACH Qualitative Study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
2.	I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my legal rights being affected.	
3.	I am willing to talk with a member of the research team about my experiences and views on the diagnosis, management and treatment of patients with COVID-19 and antibiotic usage.	
4.	I give permission for my interview with the researcher to be audio-recorded.	
5.	I understand that information collected about me during the interview will be treated with the strictest confidentiality and may be listened to by the research team and an external transcription company. The recording will not be labelled with my name.	
6.	I understand that what I say in the interview may be quoted word for word in publications, presentations and reports, but the quote will be anonymous.	
7.	I understand that information collected about me will be held at the Centre for Trials Research, Cardiff University according to the UK GDPR, the retained EU law version of the General Data Protection Regulation ((EU) 2016/679). I understand that this information will be kept strictly confidential and that no personal information will be used in the study report or publications.	
8.	I agree to regulatory authorities and University of Leeds (sponsor) accessing the data obtained in this study where it is relevant to my taking part in research, on the understanding that all data will remain confidential.	
9.	I agree to take part in the above Qualitative Study.	



Interview Topics Overview (Health Care Professionals)

The topic guide will include overarching topics we would like to cover, but will be flexible and allow the interview to be guided by interviewee in terms of order and wording, and allow the interviewee to initiate and develop topics that have not been pre-empted in advance.

INTRODUCTION:

Thank you for taking the time to speak to me today. My name is Josie. I'm not a clinician or a health professional, I'm a qualitative researcher at the Centre for Trials Research at Cardiff University. The sort of research I do involves speaking to people – often patients and health professionals – to find out about their feelings and experiences, ask them what is important to them, and ask them to describe it in their own words. I'm interested to hear what your views on the challenges and issues you faced and still face treating patients with suspected COVID and particularly about antibiotic use.

I would like to hear about your experiences and your opinions in your own words and there are no right or wrong answers. Anything you say will be really helpful. If you need to stop the interview then please feel free to say so at any time. Do you have any questions before we get started?

Consent script

Could you talk to me about your role (or your role from last year April 2020 to July 2020 if it's changed), for instance, what sort of hospital, ward, patients do you work with?

How long have you been in your role and how senior are you?

A. Antibiotic decision making

1. Extent of first wave of COVID-19 in your hospital – our dates are April 2020 to July 2020, but yours might be different – what was it like?
2. How did you decide whether patients hospitalised with COVID-19 needed to start antibiotics?
3. How do you decide which antibiotics to prescribe?
4. How do you decide when to stop or review antibiotics?
5. What clinical factors influenced your decision to start or stop or change antibiotics? e.g type/severity/duration of symptoms, follow on Q: do laboratory/test results have a role?



Or How important do you think laboratory or test results were to antibiotic prescribing decisions in COVID-19?

What impact would time to receive test results have on your decision-making? e.g. bedside test or sent to lab?

6. What non-clinical factors influenced your decision to start or stop or change antibiotics? e.g family, ethnicity, social support, home environment, late presentation, space on the ward(s), clinician's personal attitude to risk, previous experience, second opinion

B. Clinical guidelines (NB centres might have 'pathways', or 'algorithms'; these may be built into guidelines) [Explain 'guidelines' will be used to encompass all these resources].

1. In your hospital, did you routinely use a guideline to assist the decision to start or stop antibiotics in patients with COVID-19?

2. Guidelines: How useful were the guidelines? Did you overrule them? How often? What prompted you to do this? Did you consult more than one guideline?

- How did you combine the guidelines with your own clinical judgement? How did you use guidelines to make decisions?
- How could you improve the guidelines?
- How early were the guidelines introduced? How was it shared and disseminated throughout clinical teams? Did your use of the guideline change over time?

Did your guideline/practice involve procalcitonin testing?

3. PCT

If yes, PCT test used during first wave

- How did you use the PCT test? E.g what part of the hospital? ICU, emergency department? Mainstream ward?
- Did you find the PCT test useful? What were the advantages of using the test?
- Has the extent to which you find it useful changed over the course of pandemic, or how confident are you in using compared to before?
- What were the disadvantages of using the test? What were the barriers to using the test?
- What is your personal experience of using PCT test before COVID-19? If PCT test only introduced during COVID-19: Can you imagine using the PCT test in everyday practice, after pandemic?
- Was use of PCT included in guidelines?
- Algorithm guidelines: How useful were the guidelines produced by the algorithm? Did you agree with the way in which the algorithm interpreted the PCT test results? Did you interpret the test results in a different way to the algorithm? Did you overrule the test results? How often? When?
- How did you combine the test result with your own clinical judgement? How did you use the test result to make decisions?
- What were patients' perceptions of using the PCT test? Did you use the test results and/or guidelines in discussions with patients?
- Do you think the use of PCT testing safely reduced antibiotic use among patients hospitalised with COVID-19? Where there other benefits in terms of antibiotic use?

If no PCT test and/or algorithm not used during first wave



- Do you think the introduction of (or more frequent/accessible?) PCT testing would be useful to support your clinical decision to stop and start antibiotics in patients with suspected COVID? Where do you think PCT could be most useful?
- Do you think the introduction of algorithm would be useful to support your clinical decision to stop and start antibiotics in patients with suspected COVID? Would you use one if it were introduced? What features do you think would be useful?
- Do you think the use of PCT testing could safely reduce antibiotic use among patients hospitalised with COVID-19?

NICE guidelines

What impact did NICE COVID-19 rapid guideline have on your Trust's decision about PCT use?

Attitude to PCT generally

Has your view of PCT changed during COVID-19?

Lessons learned?

- Thinking back in time to the busiest time during the first wave of COVID in spring 2020, do you think there are things that could have improved your practice and management of antibiotic use in patients?
- Are there lessons you learned that you took with you as COVID cases increased during winter 2020 and beyond? Have you noticed changes in your colleagues' thinking and behaviours?

Scenario: I'm going to share with you a case study with complexities where decision making is not straight forward. I'll then ask you to describe what your decision making would be around starting and stopping antibiotics.

78 years old female, white, BMI 18, admitted this morning

Unconfirmed COVID-19, awaiting test results

Symptoms started 3 days ago: fever (39.2C), loss of taste and diarrhoea

No significant shortness of breath, but respiratory rate increased to 22/min

SpO2 91% without oxygen. CXR shows bilateral pulmonary infiltrates – typical of COVID-19. Bloods: neutrophilia and raised CRP, elevated urea and creatinine (previously normal), Hb 92

PMHx: ischaemic heart disease, hypertension, renal impairment with reduced eGFR, known microcytic anaemia on Fe supplement

Explore with clinician how events and decisions occurred over time.

What clinical factors influenced your decision on starting and stopping antibiotics?

What other (non-clinical) factors influenced your decision on starting and stopping antibiotics?

How might this differ with a less complex patient case?

Then add:

Patient does not handle anti-biotics well.

History of C Difficile



Family involvement

Closing

- Is there anything you'd like to add that you think is relevant or important that you haven't had a chance to bring up yet?

PEACH Study Group

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